(3) Claims 1, 3, 25, 28, and 30 stand rejected under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,519,635 to Miyake et al.;

(4) Claims 1-12, 25,26, 28 and 30 stand rejected under 35 U.S.C. §103(a) as obvious over WO 97/44132 (Loux et al.) in view of U.S. Patent No. 4,935,040 to Goedert; and

(5) Claims 2, 4-12, 26 and 30 stand rejected under 35 U.S.C. §103(a) as obvious over Miyake et al. in view of Swedberg et al.

The aforementioned grounds of rejection are addressed in part by the present amendments and are otherwise traversed for reasons that will be discussed in detail herein. In addition, a proposed new Fig. 7C is submitted herewith. Furthermore, claims 1, 25, 26, and 28 have been amended. Accordingly, claims 1-8, 10-12, 25, 26, 28 and 30 are now pending.

**THE ABOVE CLAIM AMENDMENTS:**

Amended independent claims 1, 25 and 28 set forth that the invention relates to a microdevice that includes a plurality of separation units, each having a microchannel of a different length, and a reservoir unit having dimensions that enable its operative and modular coupling to the separation units in succession. Each claim also recites an external power source capable of generating an electric field difference between ***electrically conductive probes*** extending into the reservoir unit. When the power source is operatively connected to the reservoir unit, liquid from the reservoir unit is ***electrokinetically driven*** by an electric field difference between the probes into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

Support for these amended independent claims can be found throughout the application as filed. For example, it is disclosed on page 1, line 13, to page 3, line 4, that the invention relates to an apparatus that uses microfluidic planar columns or capillaries to carry out chromatographic separation. In addition, it is disclosed that the invention allows for the successive coupling of the separation units with the reservoir unit because, as discussed on page 3, line 19 to page 4, line 2 and on page 5, line 22, to page 6, line 7, the modular nature of the invention allows for the substitution of different components, e.g., separation units having microchannels of different lengths, to accommodate the specific needs associated with analyzing a particular sample.

Furthermore, it is disclosed on page 3, line 10, to page 4, line 2, that an analyte may be driven by an external power source through a microchannel of the inventive device and that the time in which it takes for the analyte to pass through the microchannel is indicative of the molecular characteristics of the analyte. According to the specification on page 12, lines 3-10, the power unit may have probes to provide energy to drive liquid or chemical analyte electrokinetically through the microchannel in a manner typified by capillary electrophoresis. As discussed on page 17, lines 18-22, the probes may be electrically conductive and extend into the reservoir unit. The probes are depicted, for example, in Fig. 1 and indicated by reference numerals 112A, 112B, 112C, and 112D. Thus, these amended independent claims are fully supported by the original disclosure of the application, and no new matter has been added.

Claim 9 has been cancelled to eliminate duplicative recitation of claim elements, and claim 26, previously depending from claim 9, has been amended to depend from claim 2. These minor amendments do not introduce any new matter.

Thus, upon entry of this amendment, claims 1-8, 10-12, 25, 26, 28, and 30 are pending. For the Examiner's convenience, pending claims are listed in Appendix C.

**OBJECTION TO DRAWINGS:**

The Examiner objected to applicants' submission of a revised Fig. 7B and required submission of a new Fig. 7C. In the interest of expediting prosecution, applicants have proceeded under the assumption that the previously proposed changes to Fig. 7B were not entered and now submits a proposed new drawing, Fig. 7C, which depicts a reservoir unit with two separation units with microchannels of different lengths.

A new paragraph setting forth a brief description of Fig. 7C has been added to page 5 of the specification, and text on page 11, lines 11-17, has been amended to correspond to the new figure. As discussed in the applicants' previous communication, the new figure and accompanying amended text merely reiterate subject matter that has already been disclosed in the application as filed. No new matter has been introduced in Fig. 7C or in the accompanying text.

**REJECTION UNDER 35 U.S.C. §112, FIRST PARAGRAPH:**

Claims 28 and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. Specifically, the Examiner stated that claim 28 still indicates that a plurality of separation units may be simultaneously coupled to the single reservoir. Furthermore, the Examiner stated that Figs. 1, 2, 7B and 8 indicate the use of a single separation unit connected to the reservoir unit.

Applicants disagree since claim 28 does not mention any type of simultaneous coupling between the reservoir unit and separation units. Instead, it is set forth that the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession. With applicants' submission of new Fig. 7C, it should be clear that claims 28 and 30 are directed to an apparatus that employs successive rather than simultaneous coupling of the reservoir unit to each of the separation units. Accordingly, withdrawal of the rejection is warranted.

**THE REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH:**

Claims 28 and 30 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter that applicants regard as the invention. Specifically, the Examiner states that recitation of a reservoir unit containing a liquid for introduction into the microchannels of separation units conflicts with the wherein clause reciting the successive coupling of the reservoir unit to the separation units.

With the amendments to claim 28, all ambiguities have been removed from claims 28 and 30. As these claims are definite, withdrawal of the rejection is requested.

**THE 35 U.S.C. §102(B) REJECTION OVER MIYAKE ET AL.:**

Claims 1, 3, 25, 28 and 30 stand rejected as anticipated by Miyake et al. In issuing this rejection, the Examiner contends that Miyake et al. teaches an apparatus for chemical analysis with multiple detachable separation units. Pointing to Figs. 6-8 and citing column 9, line 65, to column 10, line 18, the Examiner states that separation units may have channels of different lengths. In particular, the Examiner points to the presence of mixing channel 116 in the

separation unit of Fig. 2 and the absence of such a mixing channel in the device of Figs. 6 and 7 as supporting the proposition that the separation units of Miyake et al. may have microchannels of different lengths. In addition, the Examiner states that "the 'channel' of the instant invention does not comprise any structure elements of any means to create solute retention which would distinguish it from the 'channel' of Miyake et al."

Applicants disagree because Miyake et al. does not disclose each and every element recited in the pending claims. The pending claims are directed to modular microdevices in which microchannels form separation columns or capillaries of different lengths. Clearly, separation columns or capillaries of different lengths are structural elements, rather than mere intended-use limitations. Contrary to the Examiner's assertion, the mixing channel 116 in Fig. 2 of Miyake et al. does not serve as a separation column or capillary. Instead, chromatocolumn 115 of Miyake et al. is the item most akin to a separation column or capillary, as recited in the pending claims. As depicted in Miyake et al., all chromatocolumns 115 have the same length and shape. Accordingly, applicants maintain that although Miyake et al. arguably discloses separation columns or capillaries of the same size and shape, separation columns or capillaries of different lengths are not disclosed.

In addition, all independent claims now set forth that the invention relates to microdevices that use an electric field difference between conductive probes to effect electrokinetic flow. In contrast, Miyake et al. does not disclose microdevices that include electrically conductive probes. Instead, the devices of Miyake et al. rely on ordinary mechanical pumps to generate fluid flow. Thus, unlike the subject matter of the pending claims, the devices of Miyake et al. cannot carry out electrokinetic-flow-based separation processes.

Since Miyake et al. does not disclose electrically conductive probes for generating electrokinetic flow or modular separation units having columns or capillaries of different lengths, the pending claims do not read on the Miyake et al. Accordingly, applicants request withdrawal of this rejection.

**THE 35 U.S.C. §103(A) REJECTION OVER LOUX ET AL. IN VIEW OF GOEDERT:**

Claims 1-12, 25, 26, 28 and 30 stand rejected as obvious over Loux et al. in view of Goedert. The Examiner states that Loux et al. teaches a modular housing assembly for a

micromachined fluid handling structure that may use a plurality of replaceable separation units. The Examiner also states that Loux et al. teaches the use of a single reservoir unit with a membrane in conjunction with the separation units, modular heater assembly and power units. Although the Examiner states that Loux et al. does not disclose a separation device comprising a first and second half, the Examiner states that Goedert teaches separation units formed from first and second planar halves. Accordingly, the Examiner maintains that it would have been obvious to combine the teachings of Loux et al. and Goedert to provide a unitary device for sample separation that provides increased flexibility, reliability, speed and precision of operation.

As an initial matter, Loux et al. and Goedert both relate to miniature devices that employ pneumatic pressure in order to effect gaseous or liquid flow. As a result, even if Loux et al. and Goedert were properly combinable, they would not teach a microdevice that includes electrically conductive probes to effect electrokinetic flow. In addition, as recognized by the Examiner, these two references would teach the use of a ***unitary*** separation unit having a serpentine microchannel and a plurality of chromatographic columns. Clearly, a single unitary separation unit can only be repeatedly, but not successively, coupled to a reservoir unit. In effect, then, disclosure relating to a unitary separation unit teaches away from the inventive subject matter, which relates to a plurality of separation units. Thus, Loux et al. and Goedert do not disclose or suggest the subject matter of the pending claims, i.e., an apparatus having a plurality of separation units each having a separation column or capillary of a different length for successive coupling to a single reservoir unit. Accordingly, applicants request reconsideration and withdrawal of this rejection as well.

**THE 35 U.S.C. §103(A) REJECTION OVER MIYAKE ET AL. IN VIEW OF SWEDBERG ET AL.:**

Claims 2, 4-12, 26 and 30 stand rejected as obvious over Miyake et al. in view of Swedberg et al. In support of the rejection, the Examiner repeated substantially the same reasoning as that previously employed.

Applicants submit that the Examiner's reasoning is flawed here as well. As discussed above, the claims are generally directed to an apparatus having a plurality of separation units each having a separation column or capillary of a different length for successive coupling to a single reservoir unit. Neither reference discloses or suggests separation units each having a

separation column or capillary of a different length for successive coupling to a single reservoir unit. In addition, in order to effect flow in the separation units as set forth in the pending claims, an electric field difference is applied to electrically conductive probes that extend into the reservoir unit so as to effect electrokinetic flow of fluid from the reservoir unit and through the separation units. Since electrically conductive probes of a external power source that extend into a reservoir unit are neither disclosed nor suggested by Miyake et al. or Swedberg et al, applicants request reconsideration and withdrawal of this rejection as well.

## CONCLUSION

For all of the above reasons, it is submitted that the application comports with all requirements of 35 U.S.C. §112, and that the pending claims define an invention that is patentable over the art. As the application should now be in condition for allowance, a prompt indication to that effect would be appreciated.

If the Examiner has any questions concerning this communication, she is welcome to contact Michael Beck at (650) 485-3864.

Respectfully submitted,

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## APPENDIX A
## AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph on page 5, after line 14 and before lines 15-16.

Fig. 7C shows an exploded isometric view of an embodiment of a reservoir unit capable of being coupled to two separation units in succession according to the invention.

Please amend the paragraph on page 11, lines 11-17, as follows:

Alternatively, as shown in Fig. 7B, the reservoir unit 104B can be made such that the reservoirs (e.g., 106K) have a bottom (e.g., 106L), which is thin so that it can be punctured by a protrusion arm 106M from the separation ~~units~~ unit 102B ~~or 102C in succession~~. The protrusion arms 106M each can have a channel for allowing fluid to flow from the reservoir into the separation unit 102B ~~or 102C~~. It is preferred that the reservoir unit 104 is made of a material that can seal against the separation unit 102B ~~or 102C~~ well to prevent leakage.

Fig. 7C. depicts the same device as Fig. 7B except that an additional separation unit 102C is employed. Thus, the reservoir unit 104B can be made such that the reservoirs (e.g., 106K) have a bottom (e.g., 106L), which is thin so that it can be punctured by a protrusion arm 106M from the separation units 102B or 102C in succession. As shown, separation units 102B and 102C have channels of different lengths.

## APPENDIX B
## CLAIM AMENDMENTS

1. (Amended Seven Times) A modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is of a different length and forms a separation column or capillary that separates the analyte from the sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a reservoir that contains a liquid for introduction into each of the microchannels of the separation units in succession; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes extending into the reservoir unit, the power source operatively connected to the reservoir unit for electrokinetically driving the liquid from the reservoir through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession to allow liquid from the reservoir to be electrokinetically driven, by ~~the external power source~~a power-source-generated electric field difference between the probes,-into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

25. (Amended Six Times) A kit for making a modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is of a different length and forms a separation column or capillary that separates the analyte from the sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a reservoir that contains a liquid for introduction into each of the microchannels of the separation units in succession; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes and having dimensions that enable its modular and operative

connection to the reservoir unit for electrokinetically driving the liquid from the reservoir through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession, ~~and~~ the probes extend into the reservoir unit when the reservoir unit is operatively coupled to the external power source, and a power-source-generated electric field difference between the probes ~~to drive~~ electrokinetically drives liquid from the reservoir into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

26. (Amended) The apparatus according to claim ~~9~~2, further comprising a support plate for operatively and modularly coupling to the separation units.

28. (Thrice Amended) A modular microdevice for analyte analysis, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is of a different length and forms a separation column or capillary that separates an analyte from a sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a plurality of reservoirs, wherein each reservoir contains a liquid, and each liquid is suitable for introduction into a microchannel of a separation unit; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes extending into the reservoir unit, the power source operatively connected to the reservoir unit for electrokinetically driving liquids from the reservoir unit through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession to allow liquid from at least one of the plurality of reservoirs to be electrokinetically driven, by ~~the external power source~~ a power-source-generated electric field difference between the probes, into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

## APPENDIX C
## PENDING CLAIMS UPON ENTRY OF THE AMENDMENT

1. (Amended Seven Times) A modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is of a different length and forms a separation column or capillary that separates the analyte from the sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a reservoir that contains a liquid for introduction into each of the microchannels of the separation units in succession; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes extending into the reservoir unit, the power source operatively connected to the reservoir unit for electrokinetically driving the liquid from the reservoir through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession to allow liquid from the reservoir to be electrokinetically driven, by a power-source-generated electric field difference between the probes, into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

2. An apparatus according to claim 1, wherein at least one of the separation units is chip-shaped and formed from a first half and a second half each having a substantially planar surface facing and joining the other half, wherein at least one of the planar surfaces has a channel thereon such the joining of the two surfaces forms the microchannel.

3. An apparatus according to claim 1, wherein at least one of the separation units has one or more openings leading to the microchannel capable of admitting liquid reagents such that when the separation unit and the reservoir unit are operatively and modularly coupled, the openings are aligned with the reservoirs thereby allowing the liquid reagents and the analyte to pass from the reservoirs into the microchannel without substantial leakage.

4. An apparatus according to claim 2, wherein at least one of the separation units includes a substrate comprised of a material other than silicon or silicon dioxide in which the first microchannel is formed by laser ablation.

5. An apparatus according to claim 2, wherein the reservoir unit includes a membrane that covers at least one of the reservoirs confining the prepackaged liquid reagent therein, wherein the membrane is penetrable with a probe for applying a driving force to drive movement of liquid reagent and analyte from the reservoir through the microchannel of at least one of the separation units.

6. An apparatus according to claim 2, wherein both substantially planar surfaces of the separation unit having a first half and a second half have a laser-ablated channel thereon and the two channels join to form the microchannel.

7. An apparatus according to claim 2, wherein the channel of at least one separation unit is formed by laser ablation.

8. An apparatus according to claim 2, wherein the external power unit comprises a powering plate operatively and modularly coupled to the reservoir unit, the powering plate having an electrical connection to the reservoir to provide a driving force to drive movement of the liquid reagents and analyte from the reservoir through the microchannel.

10. An apparatus according to claim 26, further comprising a peltier plate operatively and modularly coupled to the support plate for controlling the temperature of at least one of the separation units.

11. An apparatus according of claim 10, wherein the peltier plate can be used to heat or cool at least one of the separation units by selecting an appropriate mode of operation.

12. An apparatus according to claim 11, further comprising a heat exchanger operatively connected to the peltier plate to transfer heat between the peltier plate and the surrounding environment.

25. (Amended Six Times) A kit for making a modular microchannel apparatus for the chemical analysis of an analyte in a sample, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is of a different length and forms a separation column or capillary that separates the analyte from the sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a reservoir that contains a liquid for introduction into each of the microchannels of the separation units in succession; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes and having dimensions that enable its modular and operative connection to the reservoir unit for electrokinetically driving the liquid from the reservoir through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession, the probes extend into the reservoir unit when the reservoir unit is operatively coupled to the external power source, and a power-source-generated electric field difference between the probes electrokinetically drives liquid from the reservoir into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

26. (Amended) The apparatus according to claim 2, further comprising a support plate for operatively and modularly coupling to the separation units.

28. (Thrice Amended) A modular microdevice for analyte analysis, comprising:

(a) a plurality of separation units each comprised of a solid substrate having a microchannel present in the surface thereof, wherein the microchannel in each separation unit is

of a different length and forms a separation column or capillary that separates an analyte from a sample according to the molecular characteristics of the analyte;

(b) a single reservoir unit in the form of a plate comprised of a plurality of reservoirs, wherein each reservoir contains a liquid, each liquid is suitable for introduction into a microchannel of a separation unit; and

(c) an external power source capable of generating an electric field difference between electrically conductive probes extending into the reservoir unit, the power source operatively connected to the reservoir unit for electrokinetically driving liquids from the reservoir unit through the microchannels of the separation units,

wherein the reservoir unit has dimensions that enable the operative and modular coupling of the reservoir unit to each separation unit in succession to allow liquid from at least one of the plurality of reservoirs to be electrokinetically driven, by a power-source-generated electric field difference between the probes, into the microchannel of the separation unit that is operatively and modularly coupled to the reservoir unit.

30. The modular microchannel apparatus system of claim 28, wherein each of two separation units of the plurality has a microchannel of a different size.